

Claims

What is claimed is:

1. A method for inhibiting, treating, or preventing an angiogenesis-mediated disease or condition of the retina or choroid in a mammal, comprising administering to the mammal with the angiogenesis-mediated disease or condition an amount effective to inhibit, reduce, or prevent angiogenesis of a composition comprising an immunophilin binding active agent.
2. The method of claim 1 wherein said mammal is human.
3. The method of claim 1 wherein the angiogenesis-mediated disease or condition is selected from the group consisting of choroidal neovascularization, diabetic retinopathy, macular degeneration, and age-related macular degeneration.
4. The method of claim 3, wherein the angiogenesis-mediated disease or condition is selected from the group consisting of choroidal neovascularization, and exudative age-related macular degeneration.
5. The method of claim 4 wherein the angiogenesis-mediated disease or condition is choroidal neovascularization.
6. The method of claim 5 wherein said composition comprises rapamycin.
7. A pharmaceutical composition comprising: a therapeutically effective[✓] amount of rapamycin, a rapamycin analog, or tacrolimus and a pharmaceutically acceptable carrier suitable for administration to the eye or eye tissue.
8. The composition of claim 7 comprising a therapeutically effective amount of rapamycin.
9. A method for reducing angiogenesis in an animal retinal or choroidal tissue comprising, contacting said tissue with the pharmaceutical composition of claim 7.

10. A method for inhibiting or preventing angiogenesis in an animal retinal or choroidal tissue, comprising contacting said tissue with the pharmaceutical composition of claim 8.

11. A method of improving the ocular vision in retinal disorders of the mammalian eye, said disorders characterized by choroidal neovascularization or angiogenesis of the retina, said method comprising administering rapamycin, a rapamycin analog, or tacrolimus to the eye of the mammal.

12. The method of claim 11, wherein rapamycin, a rapamycin analog, or tacrolimus is administered by a mode of administration selected from the group consisting of intraocular injection, subretinal injection, subcleral injection, intrachoroidal injection, subconjunctival injection, topical administration, oral administration and parenteral administration.

13. The method of claim 11, wherein the choroidal neovascularization occurs in retinal or subretinal disorders of age-related macular degeneration, presumed ocular histoplasmosis syndrome, myopic degeneration, angioid streaks or ocular trauma.

14. The method of claim 11 wherein said mammal is human.

15. The method of claim 9 wherein said mammal is human.

16. The method of claim 10 wherein said mammal is human.

17. The method of claim 1, wherein rapamycin, a rapamycin analog, or tacrolimus is administered by a mode of administration selected from the group consisting of intraocular injection, subretinal injection, subcleral injection, intrachoroidal injection, subconjunctival injection, topical administration, oral administration and parenteral administration.

18. The method of claim 1 wherein said immunophilin binding active agent is rapamycin, a rapamycin analog, or tacrolimus.

19. The method of claim 1 further comprising the administration of another agent for the treatment of angiogenesis or neovascularization.

20. The method of claim 19 wherein said neovascularization is CNV.

21. The method of claim 20 wherein said agent is selected pyrrolidine, dithiocarbamate (NF κ B inhibitor); squalamine; TPN 470 analogue and fumagillin; PKC (protein kinase C) inhibitors; Tie-1 and Tie-2 kinase inhibitors; inhibitors of VEGF receptor kinase; proteasome inhibitors such as VelcadeTM (bortezomib, for injection; ranibuzumab (LucentisTM) and other antibodies directed to the same target; pegaptanib (MacugenTM); vitronectin receptor antagonists, such as cyclic peptide antagonists of vitronectin receptor-type integrins; α -v/ β -3 integrin antagonists; α -v/ β -1 integrin antagonists; thiazolidinediones such as rosiglitazone or troglitazone; interferon, including γ -interferon or interferon targeted to CNV by use of dextran and metal coordination; pigment epithelium derived factor (PEDF); endostatin; angiostatin; anecortave acetate; acetamide; triamcinolone; tetrathiomolybdate; AccutaneTM (13-*cis* retinoic acid); ACE inhibitors such as quinopril or perindozril; inhibitors of mTOR (mammalian target of rapamycin); 3-aminothalidomide; pentoxifylline; 2-methoxyestradiol; colchicines; AMG-1470; cyclooxygenase inhibitors such as nepafenac, rofecoxib, and diclofenac; t-RNA synthase modulator; metalloprotease 13 inhibitor; acetylcholinesterase inhibitor; potassium channel blockers; endorepellin; purine analog of 6-thioguanine; cyclic peroxide ANO-2; (recombinant) arginine deiminase; epigallocatechin-3-gallate; cerivastatin; analogues of suramin; and VisudyneTM and other photosensitizers.

22. The method of claim 11 further comprising the administration of another agent for the treatment of angiogenesis or neovascularization.

23. The method of claim 22 wherein said neovascularization is CNV.

24. The method of claim 23 wherein said agent is selected pyrrolidine, dithiocarbamate (NF κ B inhibitor); squalamine; TPN 470 analogue and fumagillin; PKC (protein kinase C) inhibitors; Tie-1 and Tie-2 kinase inhibitors; inhibitors of VEGF receptor kinase; proteasome inhibitors such as VelcadeTM (bortezomib, for injection; ranibuzumab (LucentisTM)

and other antibodies directed to the same target; pegaptanib (Macugen™); vitronectin receptor antagonists, such as cyclic peptide antagonists of vitronectin receptor-type integrins; α -v/ β -3 integrin antagonists; α -v/ β -1 integrin antagonists; thiazolidinediones such as rosiglitazone or troglitazone; interferon, including γ -interferon or interferon targeted to CNV by use of dextran and metal coordination; pigment epithelium derived factor (PEDF); endostatin; angiostatin; anecortave acetate; acetamide; triamcinolone; tetrathiomolybdate; Accutane™ (13-*cis* retinoic acid); ACE inhibitors such as quinopril or perindozril; inhibitors of mTOR (mammalian target of rapamycin); 3-aminothalidomide; pentoxifylline; 2-methoxyestradiol; colchicines; AMG-1470; cyclooxygenase inhibitors such as nepafenac, rofecoxib, and diclofenac; t-RNA synthase modulator; metalloprotease 13 inhibitor; acetylcholinesterase inhibitor; potassium channel blockers; endorepellin; purine analog of 6-thioguanine; cyclic peroxide ANO-2; (recombinant) arginine deiminase; epigallocatechin-3-gallate; cerivastatin; analogues of suramin; and Visudyne™ and other photosensitizers.

25. A method of visualizing or detectably labeling blood vessels of a non-human animal, said method comprising intracardiac perfusion of said animal with a lipophilic dye followed by a wash, optionally in a fixative solution.

26. The method of claim 25 wherein said fixative comprises paraformaldehyde.

27. A method of inducing neovascularization in the eye of a non-human animal, said method comprising subretinal injection of collagen or Matrigel™ into said animal.

28. A non-human animal comprising ocular neovascularization produced by the method of claim 27.

29. A method of identifying a candidate compound as inhibiting neovascularization, said method comprising administering said compound to an animal according to claim 28 and determining whether neovascularization was inhibited.